

### **Remarks**

As a result of this amendment, Claims 11-12, 15 have been canceled. Claims 10, 13 and 18 have been amended. Claims 10, 13-14, 16-18 are now pending. No new matter has been added by way of amendment.

### **Claim rejections**

Claims 11, 12, 14-18 have been rejected under 35 USC 112, second paragraph.

Applicants believe the present amendments to the claims address paragraphs 1-6 of the rejection. Regarding paragraph 4, the claim language “from position 2” is to allow substitution on any C-atom of the alkoxy carbonyl / cycloalkoxy carbonyl except for the C-atom directly linked to the oxygen. Applicants believe the amended claim language “optionally substituted, except for position 1 in relation to the oxygen atom,” renders the claims more clear.

Withdrawal of the 35 USC 112, second paragraph rejection is respectfully requested.

Claims 10-18 have been rejected under 35 USC 112, first paragraph. This rejection is traversed in part.

Applicants believe the present amendments to the claims address paragraph 1 of the rejection.

Regarding paragraph 2, Applicants disagree that the specification lacks enablement for the full scope of the instant claims. The Rc and Rd definitions in the instant claims have deleted heteroaryl. Regarding Re, the critical feature of this substituent lies in the C<sub>1-6</sub> alkoxy carbonyl or C<sub>3-7</sub> cycloalkoxy carbonyl group as defined therein and if substituted with one of the recited groups, it can be substituted on any position except for position 1

relative to the oxygen atom. The unexpected activity of the instant compounds is predictable for all substituent groups recited therein, including heteroaryl groups, at that particular position in the C<sub>1-6</sub> alkoxycarbonyl or C<sub>3-7</sub> cycloalkoxycarbonyl group.

In view of the foregoing reasons, withdrawal of the 35 USC 112, first paragraph rejection is respectfully requested.

Claims 11-12, 14 and 18 have been rejected under 35 USC 103(a) as allegedly being unpatentable over Cliff (US Patent no. 5,541,326) in view of Abou-Gharbia (US Patent no. 4,988,814). This rejection is traversed.

The compounds of the present claims possess activity against Microsomal Triglyceride-Transfer Protein (MTP) and are therefore useful for lowering the plasma concentrations of atherogenic apo B and for treating diseases related thereto. These surprising properties are imparted by the novel structural selection where in the formula (I) n = 3 or 4 combined with Re being C<sub>1-6</sub> alkoxycarbonyl or C<sub>3-7</sub> cycloalkoxycarbonyl group, wherein the carbon atom of the alkoxycarbonyl group linked to the oxygen atom is a primary or secondary carbon atom. This is neither taught nor suggested alone or combined by the prior art of record. At the analogous position on the instant formula (I) between the piperazine and the terminal -C(Rc)(Rd)(Re) group, Cliff discloses compounds where a -(CH<sub>2</sub>)<sub>n</sub>- group has n being 1 or 2, whereas the instant n is 3 or 4. Neither does Abou-Gharbia fill the gap. While the reference discloses a broad range of possible methylene groups between 1 and 6 (including the C(R4)(R5) of the reference) this pertains to compounds structurally distinct from those of the instant. In Abou-Gharbia the analogous terminal group attached to X in the reference can complete a tertiary alkoxycarbonyl, or a cycloalkoxycarbonyl where the carbon attached to oxygen is a tertiary carbon. Therefore, the difference between the instant claims and what is disclosed by the combination of references of record is not only being homologs, but also by being structural isomers. Moreover the compounds of both references possess properties distinct from those of the instant. Therefore, in analyzing the invention as a whole, neither reference teaches or suggests using this distinct class of compounds to

solve this particular problem-for lowering the plasma concentrations of atherogenic apo B.

In view of the foregoing, Applicants believe a *prima facie* case of obviousness has not been made out. Withdrawal of the 35 USC 103 rejection is therefore proper and respectfully requested.

Claim 10 has been rejected under 35 USC 102(b) as allegedly being anticipated by BE 642084.

It is believed the present amendment to the claims, particularly to Rc, obviates the rejection. Withdrawal of the rejection is therefore respectfully requested.

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